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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : John C. Smith et al.

Art Unit : 1643

Serial No. : 09/743,956

Examiner : Juliet Einsmann

Filed : April 24, 2001

Title : GENETIC POLYMORPHISMS IN THE HUMAN NEUROKININ 1 RECEPTOR
GENE AND THEIR USE IN DIAGNOSIS AND TREATMENT OF DISEASES

Commissioner for Patents
Washington, D.C. 20231

RESPONSE TO RESTRICTION REQUIREMENT

Responsive to the action mailed June 21, 2002, please amend the application as follows.

In the claims:

Add new claim 19.

A1
19. The method of claim 1, wherein the sequence is determined at all nine of the following nucleotide positions: positions 2361 and 1371 as defined by the positions in SEQ ID NO:1; 271 and 272 as defined by the positions in EMBL ACCESSION NO. X65179; and 245, 461, 495, 461, 495, 600, and 809 as defined by the position in EMBL ACCESSION NO. X65181.

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I hereby certify under 37 CFR §1.8(a) that this correspondence is being deposited with the United States Postal Service as first class mail with sufficient postage on the date indicated below and is addressed to the Commissioner for Patents, Washington, D.C. 20231.

August 21, 2002
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REMARKS

Claims 1-19 are now pending in the application, new claim 19 having been added by the above amendment. Support for this claim can be found in claim 1 as originally filed, as well as on page 6, lines 23-24 of the specification.

In response to the restriction requirement mailed June 21, 2002, Applicants elect the invention of the group within Groups 1-9 (*i.e.*, covering claims 1-5) that specifies the diagnosis of a single nucleotide polymorphism at position 245 as defined by the position in EMBL ACCESSION NO. X65181. However, this election is made with traverse.

First, Applicants submit that the restriction is improper under PCT Unity of Invention standards. The Examiner states that the nine polymorphisms, claimed in a Markush type format, "...do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features..." (Restriction Requirement at page 4). The Examiner asserts that the nine polymorphisms lack a common structure, citing Section (f)(i)(B)(1) of Annex B of the Administrative Instructions under the PCT. Additionally, citing Section (f)(i)(A), the Examiner asserts that the polymorphisms of Groups 1-9 lack a common property or activity, and therefore fail to have unity of invention. Applicants maintain that the Examiner has misinterpreted the Administrative Instructions, and that in fact the nine claimed polymorphisms should be examined together.

Rule 13.2 of the PCT states,

Where a group of inventions is claimed in one and the same international application, the requirement of unity of invention referred to in Rule 13.1 shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

The examiner references Hopkins et al. (1991) as evidence that the "common structure" of the methods of Groups 1-9 is not a contribution over the prior art. This reference describes the cloning of the human Neurokinin 1 Receptor (NK1R) gene, but does not address the concept of polymorphisms. Applicants submit that the "special technical feature" shared by all of the

polymorphisms of claim 1, and that defines a contribution that each of the polymorphisms considered as a whole makes over the prior art, is the following: a polymorphism in the published NK1R gene. This becomes clear when one carefully considers the standards set out in Section (f) of Annex B of the Administrative Instructions under the PCT, concerning claims in Markush format.

Section (f) of Annex B states in part (emphasis added),

"Markush Practice." The situation involving the so-called "Markush practice" wherein a single claim defines alternatives (chemical or non-chemical) is also governed by Rule 13.2. In this special situation, the requirement of a technical interrelationship and the same or corresponding special technical features as defined in Rule 13.2, shall be considered to be met when the alternatives are of a similar nature.

(i) When the Markush grouping is for alternatives of chemical compounds, they shall be regarded as being of a similar nature where the following criteria are fulfilled:

- (A) all alternatives have a common property or activity, and
- (B)(1) a common structure is present, *i.e.*, a significant structural element is shared by all of the alternatives, or
- (B)(2) in cases where the common structure cannot be the unifying criteria, all alternatives belong to a recognized class of chemical compounds in the art to which the invention pertains.

Thus, if the criteria of paragraph A and either paragraph B(1) or B(2) are fulfilled, the members of the Markush group will be regarded as being "of a similar nature" and thus having the requisite "same or corresponding special technical features."

Section (f)(ii) of Annex B interprets paragraph (B)(1):

(ii) In paragraph (f)(i)(B)(1), above, the words "significant structural element is shared by all of the alternatives" refer to cases where the compounds share a common chemical structure which occupies a large portion of their structures... The structural element may be a single component or a combination of individual components linked together.

Likewise, Section (f)(iii) of Annex B interprets paragraph (B)(2):

(iii) In paragraph (f)(i)(B)(2), above, the words "recognized class of chemical compounds" mean that there is an expectation from the knowledge in the art that members of the class will behave in the same way in the context of the claimed invention. In other words, each member could be substituted one for the other, with the expectation that the same intended result would be achieved.

Applicants submit that in accordance with Section (f)(i)(A) of Annex B, all of the alternative polymorphisms of claim 1 do have a common property: all alternatives are nucleic acid polymorphisms in the same gene. Furthermore, in accordance with Section (f)(i)(B)(1), the nine polymorphisms of claim 1 all share a common structure in that they are all nucleic acids. More specifically, and in accordance with the explanation in Section (f)(ii), the common structural element, *i.e.*, nucleic acid, is a combination of individual components, *i.e.*, nucleotides, linked together by their sugar-phosphate backbone. This backbone clearly "occupies a large portion of their structures," as specified in Section (f)(ii). Because the criteria of both sections (f)(i)(A) and (f)(i)(B)(1) are met, the polymorphisms are clearly "of a similar nature" and so have a "technical relationship" involving "one or more of the same or corresponding special technical features" (Section (f) and Rule 13.2), the special technical feature being polymorphisms in the NK1R gene. Furthermore, Applicants note that the nine polymorphisms also meet the alternative criterion for "being of a similar nature" under Section (f)(i)(A) plus (f)(i)(B)(2), in that the polymorphisms all belong to a "recognized class of chemical compounds:" they are all nucleic acids, and also can be categorized as polymorphisms in the human NK1R gene. Thus, regardless of whether one applies the criteria of Section (f)(i)(A) in combination with paragraph (f)(i)(B)(1) or paragraph (f)(i)(B)(2), the point is made: there is unity of invention among all of the polymorphisms of claim 1.

Applicants submit that the nine polymorphisms of claim 1 satisfy the requirements of Section (f)(i) of Annex B of the Administrative Instructions, and therefore satisfy PCT Rules 13.2 and 13.1.

In addition to the above arguments based on the PCT Unity of Invention Rules, Applicants ask the Examiner to reconsider the restriction requirement on other grounds. First, since the method of treatment of claim 13 includes a diagnosis step based upon the method as claimed in claim 1 (and claim 13 could have been written as dependent on claim 1 with no change in scope), it appears that the search carried out with respect to claim 1 will reveal prior art relevant to claim 13 as well. Applicants submit that there would be no burden whatsoever on the Examiner if one were to include claim 13 in the same group as claims 1-5.

Second, it would appear that the inventions of claims 17-18 could readily be examined with that of claims 1-5, as a single search of the NK1R gene sequence should suffice. In fact, claims 17 and 18 describe the polymorphisms in the same terms as does claim 2.

Third, Applicants point out that claim 1 recites determining the sequence "at one or more" of the nine nucleotide positions. If the restriction requirement restricting the nine polymorphisms into nine separate groups is allowed to stand, it will limit applicants to claiming a method of determining the sequence at only a single one of the nine positions. The restriction requirement ignores those embodiments of the claims in which the sequence at two (or three, or four, up to nine) positions is determined. It essentially prohibits applicants from presenting claims limited to such embodiments in this application or any divisional. An example of such a claim is submitted as new claim 19 above. As this claim is dependent on claim 1, it must be included in the elected group. However, it clearly will require examination of all nine polymorphisms. Applicants fail to see how the restriction requirement, as presently formulated, can stand in view of new claim 19.

Applicants strongly protest and request withdrawal of the restriction requirement, at least with respect to restricting among the nine polymorphisms.

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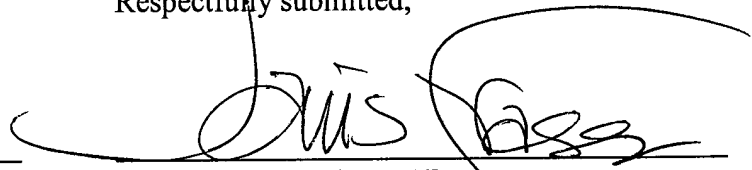
Attorney's Docket No. 06275-272001 / SAD/LDSG/Z
70365/UST

Enclosed is a Petition for Extension of Time for one month and a check for the required fee of \$110. Please apply any other charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

Date:

Aug 21, 2002



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